Journal of Forensic and Legal Medicine 20 (2013) 1–5

Contents lists available at SciVerse ScienceDirect

Journal of Forensic and Legal Medicine

journal homepage: www.elsevier.com/locate/jflm

Review

Fatal embolic events in childhood

Roger W. Byard MD, Forensic pathologist *

The University of Adelaide, Discipline of Anatomy and Pathology, Level 3 Medical School North Building, Frome Road, Adelaide 5005, South Australia, Australia

ARTICLE INFO

Article history:
Received 25 February 2012
Accepted 25 April 2012
Available online 16 May 2012

Keywords:
Thromboembolism
Tumour embolus
Children
Paradoxical embolism
Thrombophilia
Central venous catheters

ABSTRACT

Lethal embolic events in children are an uncommon occurrence that may be first detected at autopsy. Emboli consist of thrombi, tumours, infective organisms, fat, air and foreign body material. The most significant circulations that may be obstructed are the pulmonary, coronary and cerebral. Rare conditions such as arteriovenous malformations may act as sources for emboli in children, and the brain is at particular risk from paradoxical embolism. The latter is facilitated by right to left communications in the heart such as atrial and ventricular septal defects and also from pulmonary vascular abnormalities such as hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu syndrome) and arteriovenous fistulas. Iatrogenic causes of thromboembolism must be considered in children with indwelling central venous catheters and ventriculoatrial shunts. Although rare, embolic events do occur in children with lethal consequences. As the incidence of embolization in clinical settings has been increasing, due to improved survival of children with predisposing chronic conditions, it is likely that more of these cases will be the subject of forensic evaluation.

1. Introduction

Embolism refers to the transport of material in the blood stream from its origin or entry into the vasculature to a location distant to this. While it is a well recognized occurrence in adults, cases are only infrequently encountered in forensic practice in younger ages and may involve unusual conditions and mechanisms.[1] Antemortem diagnoses may not have been established. Because of these features the following review was undertaken to delineate the types of embolism that may occur in children that may result in sudden and or unexpected death, and to provide an overview of predisposing conditions. Embolic events can be subclassified a number of ways based on their composition, aetiology, origin and site of impaction (Table 1), however the most practical method groups them according to i) the particular embolic material that is involved and ii) the particular vasculature that is obstructed.

2. Thromboembolism

Emboli may be composed of a variety of different endogenous and exogenous materials. The most common embolic material consists of admixed fibrin, platelets and red blood cells, (thrombi), which arise most often within the venous circulation when one or more of the three requirements for Virchow's triad occur: stasis of blood flow, injury to the endothelial lining, and hypercoagulability of blood components.[2] As in adults, risk factors include immobility, injury, sepsis, chronic illness (including malignancy with chemotherapy), and recent surgery.[3] Other factors that play a role in childhood are congenital heart disease and central venous lines. Central venous catheters and ventriculolatrial shunts predispose to thrombosis for a number of reasons including interruption of laminar blood flow and damage to vessel endothelium.[4] These catheters have been the cause of venous thromboembolism in more than 90% of neonates and in 60% of older children.[5] Ventriculoatrial shunts may also cause lethal pulmonary hypertension.[6] Thromboemboli may arise in arteriovenous malformations in children[3] and in the dilated veins of the Klippel-Trenauney syndrome.[7,8] The risk of thromboembolism doubles in individuals with inflammatory bowel disease such as Crohn disease and ulcerative colitis, and is particularly high at young ages.[9] A similar increase in venous thromboembolism occurs in children with cystic fibrosis due to a complex interaction of a number of factors including the use of central venous catheters and an acquired thrombophilia secondary to inflammation and deficiencies in anticoagulant proteins from liver disease.[10] Other risk factors for thomboembolism in childhood include sickle cell disease, local infection and oestrogen medication.[11] As there is a definite increased risk of thromboembolism with obesity in adults[12] a high body mass index undoubtedly also has an effect on childhood thrombosis.[11]

The incidence of venous pulmonary thromboembolism has been increasing in children in recent years due to longer survival with illnesses that predispose to thromboembolic disease, and an increased use of central venous catheters.[11,13,14] In fact, a 70%

* Tel.: +618 8303 5441; fax: +618 8303 4408.
E-mail address: roger.byard@sa.gov.au.

1752-928X/$ – see front matter © 2012 Elsevier Ltd and Faculty of Forensic and Legal Medicine. All rights reserved.
doi:10.1016/j.jflm.2012.04.036

Table 1
Types of embolus and possible origin in children.

Thrombi
Central venous catheters/shunts
Cardiac valves
Intracardiac thrombi
Deep veins of the legs
Arteriovenous malformations
Tumours
Wilms tumour/nephroblastoma
Miscellaneous including pulmonary metastases
Infectious organisms
Bacteria/fungi/parasites
Fat
Soft tissues/bone marrow
Air
Vascular access catheters
Surgery
Trauma
Foreign body
Central catheters/cardiac surgery
Projectiles

increase in the annual rate of pediatric hospital admissions due to venous thromboembolism has been reported.[10]

Thrombophilic disorders are congenital or acquired conditions that lower the threshold for thrombosis resulting in an increased risk of thromboembolism.[5] Abnormalities may involve vessel endothelium and platelets, or the coagulation and fibrinolytic systems and may initiate thrombosis or may exacerbate the effect of other risk factors.[15,16] Congenital prothrombotic states include deficiencies in anti-thrombin III, plasminogen, and proteins C and S, mutations in the factor V Leiden (causing activated protein C resistance) and prothrombin genes (*G20210A*).[17] The incidence in the population may be quite high with heterozygous mutations reaching 1–7% in certain Caucasian groups. In children with venous thromboembolism the incidence of thrombophilias has ranged from 10 to 78%.[5] Although systemic lupus erythematosus (SLE) most commonly occurs in those aged between 15 and 40 years it may affect younger children and even neonates.[18] The associated antiphospholipid syndrome has been responsible for pulmonary thromboembolism as the first manifestation of SLE in a 10-year-old boy[19] and postmortem screening for these disorders in children who are found to have thromboemboli at autopsy has been proposed.[16] Pulmonary thromboembolism may also be the first manifestation of SLE due instead to lupus nephritis with nephrotic syndrome, as occurred in an 11-year-old girl with renal vein thrombosis,[20] Patients with severe proteinuria from nephrotic syndrome have a 3.4 times risk of thromboembolism.[21] Increased levels of plasma homocysteine and lipoprotein may also occur in inherited prothrombotic conditions, and increased plasma levels of factors VII, IX and XI coagulant have been associated with thromboses in children.[17]

2.1. Pulmonary

Acute obstruction of the pulmonary outflow tract is a well recognized cause of sudden collapse and death in adult populations with a variety of predisposing factors (listed above). Although less common in children, pulmonary thromboembolism does occur and may be responsible for sudden death due to acute right ventricular decompensation.[22]

Lethal pulmonary thromboembolism in children has a frequency of between 0.73% and 4.2% of cases overall but was found as a cause of death in only eight cases out of a total of 17,500 autopsies (0.05%) in one Canadian study.[3] However, this figure varies considerably among studies and populations, with embolism found to be a causal factor in the death of as many as 31% of 116 paediatric cases over a 25-year period in another study.[23]

The estimated incidence of venous thromboembolism occurring in hospitalized children is 5.3 events per 10,000 admissions, which compares to 0.07–0.14 events per 10,000 children in the community.[12] The highest rates are found in infants and children under 23 months of age and in teenage girls.[24] Although recurrent pulmonary thromboemboli are a problem in adult populations, this is less of an issue in the young with an 8.1% recurrence rate compared to 17.5% in adults. This may be a reflection of the increased number of chronic diseases in older patient groups.[25]

2.2. Coronary

While coronary artery embolism is found more often in adult autopsies, it may complicate any condition where there are friable valvular vegetations or intracavity thrombi that may disintegrate and embolize into the coronary artery circulation. Myocarditis is well recognized in childhood[26] and may result in left ventricular thrombi that give rise to coronary artery embolization and myocardial infarction.[27] Although infective endocarditis is more likely to cause sudden and unexpected death in adults[28] it has also given rise to coronary artery emboli in children.[29]

Marantic endocarditis refers to the development of noninfective vegetations on heart valves, in adults most often associated with metastatic adenocarcinoma. The vegetations are sterile and are not associated with either bacteraemia or destructive changes of the underlying valve.[30] There is a relatively high incidence of systemic embolic events and an association with lethal coronary artery or cerebral embolic events. Although predominantly a condition of older adults it may occur in children, as was reported in an eight-year-old girl with a high-grade non-Hodgkins lymphoma who suffered systemic embolization.[31] Both acute rheumatic fever and congenital heart disease may also act as a source of thromboemboli for coronary artery embolization in childhood.[32]

2.3. Cerebral

Emboli into the cerebral circulation arise either from a left-sided intracardiac source or from the right side of the heart, and venous circulation, by paradoxical embolism through a right-to-left shunt. As with coronary artery embolization left-sided lesions include valvular vegetations and thrombi from bacterial and nonbacterial endocarditis, myocarditis, rheumatic fever, myxomas, hydatid cysts and cardiomyopathy.[33–36] Other conditions that are associated with arrhythmias or infarction such as ventricular noncompaction may lead to embolization,[37] and it is known that children who have congenital and acquired cardiac disease have a fivefold risk of recurrent stroke independent of other risk factors.[38] On occasion conditions such as atrial myxoma with embolism may be associated with more widespread abnormalities such as the Carney complex with characteristic skin pigmentation and endocrine abnormalities.[39] In cases of pure thrombosis, factors such as sepsis, dehydration, cyanotic congenital heart disease and prothrombotic abnormalities have to be considered.

3. Tumour embolism

The most commonly occurring tumour embolus in children arises from Wilms tumour or nephroblastoma which results from its angioinvasive nature with direct growth into the renal vein and the inferior vena cava.[40] On occasion a tongue of tumour may extend as far as the right atrium. In such cases large segments of the tumour may fragment resulting in a saddle embolism with impaction at the bifurcation of the pulmonary artery.

Other less common angioinvasive tumours may also embolize. An example is pleuropulmonary blastoma, a high-grade sarcoma in the young which infiltrates both venous and arterial systems resulting in embolic occlusion of cerebral vessels, pulmonary veins, the aorta and the femoral artery.[41] Hepatoblastoma may embolize during surgery and cerebral metastases may arise when pulmonary metastases fragment.[42,43] Massive pulmonary haemorrhage has been reported from extensive microemboli from a gastric carcinoma.[44]

4. Septic/mycotic embolism

A wide range of infectious agents may result in embolic events in children.

4.1. Bacteria

As noted above, bacterial endocarditis can result in embolization of friable vegetations containing bacteria from cardiac valves to all parts of the peripheral vasculature. Proliferation of bacteria with associated inflammation can result in vessel occlusion or rupture from aneurysm formation.

4.2. Fungi

Proliferation of opportunistic fungi in immunocompromised children who have received chemotherapy for malignancy can result in embolization of fungal material. Those at highest risk are febrile, neutropenic children with treated acute leukaemia who have recently received antibiotics. Systemic embolization may result in occlusion of smaller arteries with back growth of fungi. A case of a six-year-old girl with acute lymphoblastic leukaemia demonstrates a typical sequence of events with embolization of *aspergillus sp*. from the lungs into a mediastinal branch of the thoracic aorta with subsequent thrombotic occlusion of the aorta.[45] Postmortem arterial blood cultures in these cases may be more likely to have a higher yield of viable fungi than venous blood that has been filtered through the capillary bed.[46]

4.3. Parasites

Thromboembolism due to parasites is found more often in tropical areas and occurs in conditions such as malaria and schistosomiasis. Rarely rupture of cardiac hydatid cysts in childhood may result in cerebral embolization with infarction, or in pulmonary embolism.[34,47] This occurs in areas of the world where the hydatid life cycle is maintained because of sheep farming.[48]

5. Fat embolism

Fat embolism is characterized by aggregates of fat within the pulmonary, cerebral and peripheral circulations following major trauma with long bone fracture. Fat embolism syndrome refers to the associated clinical manifestations that occur within 72 h of injury due to pulmonary and cerebral vessel occlusion with respiratory distress, thrombocytopaenia and deteriorating mental function.[49] Multiorgan failure and death occur in the most extreme cases. Fat embolism is found in as many as 10% of patients with pelvic and multiple long bone fractures,[49] but can also arise from soft tissue injury with crushing of adipose tissue in the absence of fractures. Although mainly occurring in adults it may be seen in children.[50] Fat embolism has also been reported in infants following prolonged intravenous lipid therapy and also in children with haemoglobinopathies and viral infections.[17]

6. Air embolism

Air may enter either the arterial or venous systems following trauma or medical procedures such as surgery, vascular catheterization and ventilation.[51,52] If sufficient air has entered the vasculature there may be sudden loss of consciousness and death due to cerebral and coronary artery obstruction.[53] The amount of air required is quite small with death resulting from an injection into the cerebral circulation of as little as 2 mls, and into the pulmonary vein of as little as 0.5–1 mls.[53] Air may enter the blood stream through arterial or venous catheters, or through bronchovenous fistulae if there has been lung trauma.[54]

A feature of blunt chest trauma at all ages, including childhood, is that there may be some delay between the tissue injury and the development of alveolar-pulmonary venous fistulae.[55,56] Air may also paradoxically pass into the arterial circulation if there is a patent foramen ovale. Neonates are at particular risk of air embolism from ventilation, as respiratory distress syndrome requires higher ventilator pressures that predispose to pulmonary parenchymal and vascular damage with leakage of air into the circulation.[54]

7. Foreign body embolism

While foreign body embolism in the forensic literature often refers to embolised fragments of bullets, a more usual event in children is embolization of part of an implanted medical device. An example is that of venous access devices that are implanted in oncology patients to facilitate repetitive venepuncture. A study of 83 catheters implanted into children and adolescents revealed embolization rates of 8 and 23% depending on the site of insertion (jugular and subclavian veins, respectively).[57] Although extraction of the embolized fragments was successfully performed in the majority of cases, embolization of material following transcatheter closure of atrial septal defects and patent ductus arteriousus may lead to life threatening complications requiring immediate surgical intervention.[58] Embolization of a wooden fragment from an exploded toy gun that had passed from the superior vena cava into the right ventricle was reported as early as 1834 in a young boy, and embolization of a shotgun pellet in a 12-year-old boy shot in the right side to the middle cerebral artery demonstrates a more recent example.[59]

8. Miscellaneous

Rarely fragments of cerebral tissue and skeletal muscle may embolize to the lung following significant trauma with massive organ and tissue disruption. These are essentially secondary phenomena that may be observed histologically following motor vehicle crashes or falls from heights. Bone marrow emboli are not uncommonly seen in microscopic lung sections when there has been external cardiac massage with rib fractures.

Paradoxical embolism occurs when a communication exists between the right and left sides of the heart in the form of a patent foramen ovale, an atrial septal defect or a ventricular septal defect. While not necessarily a problem in themselves, such defects may permit passage of embolic material into the systemic circulation with cerebral embolization. Such as case occurred with an eight-year-old boy who suffered cerebral infarction following partial surgical removal of a Wilms tumour due to paradoxical embolization through a ventricular septal defect.[60] Vascular disorders involving the lungs such as hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu syndrome) and arteriovenous fistulas may also provide conduits leading to paradoxical cerebral embolism.[61,62] It is

now considered that paradoxical embolism is an important cause of arterial ischemic stroke in children.[63]

9. Conclusion

This review has demonstrated that, although uncommon, embolization of a variety of materials may occur in children at all ages with potentially lethal consequences.[64] Embolization may be caused or facilitated by rare congenital conditions, the features of which should be carefully checked for at autopsy and family screening for hereditary thombophilias should be considered. It is also worthwhile examining the medical history in young individuals who are found at autopsy to have died from pulmonary thromboembolism as on occasion episodic shortness of breath due to previous thromoboembolic events may have been incorrectly attributed to other conditions such as asthma.[17]

Conflicts of interest
None.

Funding
None.

Ethical approval
Not applicable.

References

1. Brandão LR, Labarque V, Diab Y, Williams S, Manson DE. Pulmonary embolism in children. *Semin Thromb Hemost* 2011;**37**:772–85.
2. Esmon CT. Basic mechanisms and pathogenesis of venous thrombosis. *Blood Rev* 2009;**23**:225–9.
3. Byard RW, Cutz E. Sudden and unexpected death in infancy and childhood due to pulmonary thromboembolism. *Arch Pathol Lab Med* 1990;**114**:142–4.
4. Byard RW. Mechanisms of sudden death and autopsy findings in patients with Arnold-Chiari malformation and ventriculoatrial catheters. *Am J Forensic Med Pathol* 1996;**17**:260–3.
5. Revel-Vilk S, Kenet G. Thrombophilia in children with venous thromboembolic disease. *Thromb Res* 2006;**118**:59–65.
6. McMahon DP, Aterman K. Pulmonary hypertension due to multiple emboli. *J Pediatrics* 1978;**92**:841–5.
7. Barbara DW, Wilson JL. Anesthesia for surgery related to Klippel-Trenaunay syndrome: a review of 136 anesthetics. *Anesth Analg* 2011;**113**:98–102.
8. Jensen L, Heath K, Scott G, Byard RW. Sudden death and forensic evaluation of neurocutaneous syndromes. *J Forensic Leg Med* 2009;**16**:369–74.
9. Kappleman MD, Horvath-Puho E, Sandler RS, Rubin DT, Ullman TA, Pedersen L, et al. Thromboembolic risk among Danish children and adults with inflammatory bowel disease: a population-based nationwide study. *Gut* 2011;**60**:937–43.
10. Takemoto CM. Venous thromboembolism in cystic fibrosis. *Pediatr Pulmon* 2012;**47**:105–12.
11. Patocka C, Nemeth J. Pulmonary embolism in pediatrics. *J Emerg Med* 2012;**42**:105–16.
12. Byard RW. The complex spectrum of forensic issues arising from obesity. *Forensic Sci Med Pathol*, in press.
13. Gerotziafas GT. Risk factors for venous thromboembolism in children. *Int Angiol* 2004;**23**:195–205.
14. Johnson NN, Toledo A, Endom EE. Pneumothorax, pneumomediastinum, and pulmonary embolism. *Pediatr Clin Nth Am* 2010;**57**:1357–83.
15. Barnes C, deVeber G. Prothrombotic abnormalities in childhood ischaemic stroke. *Thromb Res* 2006;**118**:67–74.
16. Ely SF, Gil JR. Fatal pulmonary thromboembolism and hereditary thrombophilias. *J Forensic Sci* 2005;**50**:411–8.
17. Byard RW. *Sudden death in the young*. 3rd ed. Cambridge, UK: Cambridge University Press; 2010.
18. Nicklin A, Byard RW. Lethal manifestations of systemic lupus erythematosus in a forensic context. *J Forensic Sci* 2011;**56**:423–8.
19. Bhat MA, Qureshi UA, Ali SW, Bhat JI, Din N, Robbani I. Pulmonary thromboembolsim as the initial manifestation in a child with antiphospholipid syndrome in the emergency department. *Pediatr Emerg Care* 2011;**27**:205–7.
20. Skalova S, Minxova L, Lukes A, Dedek P, Tousovska K, Podhola M. Renal vein thrombosis with pulmonary embolism: first manifestation of lupus nephritis (letter). *J Pediatr Child Helath* 2011;**47**:315–6.
21. Park SJ, Shin JI. Complications of nephrotic syndrome. *Kor J Pediatr* 2011;**54**:322–8.
22. Becker RC, Graor R, Holloway J. Pulmonary embolism: a review of 200 cases with emphasis on pathophysiology, diagnosis and treatment. *Cleve Clin Quart* 1984;**51**:519–29.
23. Buck JR, Connors RH, Coon WW, Weintraub WH, Wesley JR, Goran AG. Pulmonary embolism in children. *J Pediatr Surg* 1981;**16**:385–91.
24. Stein PD, Kayali F, Olson RE. Incidence of venous thromboembolism in infants and children: data from the national hospital discharge survey. *J Pediatr* 2004;**145**:563–5.
25. Monagle P, Adams M, Mahoney M, Ali K, Barnard D, Bernstein M, et al. Outcome of pediatric thromboembolic disease: a report from the Canadian childhood thrombophilia registry. *Pediatr Res* 2000;**47**:763–6.
26. Smith NM, Bourne AJ, Clapton WC, Byard RW. The spectrum of presentation at autopsy of myocarditis in infancy and childhood. *Pathology* 1992;**24**:129–31.
27. Bor I. Myocardial infarction and ischaemic heart disease in infants and children. Analysis of 29 cases and review of the literature. *Arch Dis Child* 1969;**44**:268–81.
28. Byramji A, Gilbert JD, Byard RW. Sudden death as a complication of bacterial endocarditis. *Am J Forensic Med Pathol* 2011;**32**:140–2.
29. Celermajer DS, Sholler GF, Howman-Giles R, Celermajer JM. Myocardial infarction in childhood: clinical analysis of 17 cases and medium term follow up of survivors. *Brit Heart J* 1991;**65**:332–6.
30. Lee V, Gilbert JD, Byard RW. Marantic endocarditis and sudden death. *J Forensic Leg Med*, in press.
31. Ali N, Konstantinov I, Heath JA, Bhagwat K, Cheung M. Nonbacterial thrombotic endocarditis in a child with non-Hodgkins lymphoma. *Pediatr Cardiol*, DOI 10.1007/s00246-012-0230-y.
32. Stahl J, Santos LD, Byard RW. Coronary artery thromboembolism and unexpected death in childhood and adolescence. *J Forensic Sci* 1995;**40**:599–601.
33. Ausman JI, Diaz FG, Ma SH, Dujovny M, Sadasivan B. Cerebrovascular occlusive disease in children: a survey. *Acta Neurochirurg* 1988;**94**:117–28.
34. Byard RW, Bourne AJ. Cardiac echinococcosis with fatal intracerebral embolism. *Arch Dis Child* 1991;**66**:155–6.
35. Kelley RE. Hemorrhagic cerebral infarction in pediatric patients. *Pediatr Neurol* 1986;**2**:111–4.
36. Durgut K, Onoglu R, Gormus N. Primary cardiac myxomas: report of 28 cases and review of the literature. *J BUON* 2011;**16**:345–8.
37. Correia E, Rodrigues B, Santos L, Faria R, Ferreira P, Gama P, et al. Noncompaction of the ventricular myocardium: characterization and follow-up of an affected population. *Rev Port Cardiol* 2011;**30**:323–31.
38. Brankovic-Sreckovic V, Milic-Rasic V, Jovic N, Milic N, Todorovic S. The recurrence risk of ischemic stroke in childhood. *Med Princ Pract* 2004;**13**:153–8.
39. Stajevic MS, Vukomanovic VA, Kuburovic VD, Djuricic SM. Early recurrent left atrial myxoma in a teenager with *de novo* mutation of Carney complex. *Ind J Hum Genet* 2011;**17**:108–10.
40. Ceelen W, Kerremans I, Lutz-Dettinger N, Vandenbroeck P, de Hemptinne B. Wilms' tumour presenting as pulmonary embolism. *Acta Chir Belg* 1997;**97**:148–50.
41. Priest JR, Andic D, Arbuckle S, Gonzalez-Gomez I, Hill A, Williams G. Great vessel/cardiac extension and tumor embolism in pleuropulmonary blastoma: a report from the International Pleuropulmonary Blastoma Registry. *Peditr Blood Cancer* 2011;**56**:604–9.
42. Dorman F, Sumner E, Spitz L. Fatal intraoperative tumour embolism in a child with hepatoblastoma. *Anesthesiology* 1985;**63**:692–3.
43. Chan KW, Fryer CJH, Fraser GC, Dimmick JE. Sudden cerebral death in malignant presacral teratoma. *Med Pediatr Oncol* 1985;**13**:395–7.
44. Somers GR, Smith CR, Perrin DG, Wilson GJ, Taylor GP. Sudden unexpected death in infancy and childhood due to undiagnosed neoplasia. An autopsy study. *Am J Forensic Med Pathol* 2006;**27**:64–9.
45. Byard RW, Jimenez CL, Carpenter BF, Hsu E. Aspergillus-related aortic thrombosis. *Can Med Assoc J* 1987;**136**:155–6.
46. Byard RW. Arterial blood cultures in disseminated fungal disease. *Pediatr Infect Dis J* 1989;**8**:728–9.
47. Ilic S, Parezanovic V, Djukic M, Kalangos A. Ruptured hydatid cyst of the interventricular septum with acute embolic pulmonary artery complications. *Pediatr Cardiol* 2008;**29**:855–7.
48. Byard RW. An analysis of possible mechanisms of unexpected death occurring in hydatid disease (echinococcosis). *J Forensic Sci* 2009;**54**:919–22.
49. Bulger EM, Smith DG, Maier RV, Jurkovich GJ. Fat embolism syndrome. A 10-year review. *Arch Surg* 1997;**132**:435–9.
50. Bolliger SA, Muehlematter K, Thali MJ, Ampanozi G. Correlation of fat embolism severity and subcutaneous fatty tissue crushing and bone fractures. *TJ Leg Med* 2011;**125**(3):453–8.
51. Souders JE. Pulmonary air embolism. *J Clin Monit* 2000;**16**:375–83.
52. Matte GS, Kussman BD, Wagner JW, Sl Boyle, Howe RJ, Pigula FA, et al. Massive air embolism in a Fontan patient. *J Extra Corpor Technol* 2001;**43**:79–83.
53. Ho AM-H, Ling E. Systemic air embolism after lung trauma. *Anesthesiology* 1999;**90**:564–75.
54. Azad C, Parmar V, Aggarwal P. Massive cerebral air embolism on ante mortem CT head following pneumothorax in a child with pneumonia. *J Trop Pediatr* 2011;**57**:490–2.
55. Temlett J, Byard RW. Air embolism – an unusual cause of delayed death following gunshot wound to the chest. *Med Sci Law* 2011;**51**:56–7.
56. Brederlau J, Muellenbach RM, Wunder C, Schwemmer U, Kredel M, Roewer N, et al. Delayed systemic air embolism in a child with severe blunt chest trauma treated with high-frequency oscillatory ventilation. *Can J Anesth* 2011;**58**:555–9.

57. Ribeiro RC, Abib SCV, Aguiar AS, Schettini ST. Long-term complications in totally implantable venous access devices: randomized study comparing subclavian and internal jugular vein puncture. *Pediatr Blood Cancer* 2012;**58**:274–7.
58. Amanullah MM, Siddiqui MT, Khan MZ, Atiq MA. Surgical rescue of embolized Amplatzer devices. *J Card Surg* 2011;**26**:254–8.
59. Vascik JM, Tew Jr JM. Foreign body embolization of the middle cerebral artery: review of the literature and guidelines for management. *Neurosurgery* 1982;**11**:532–6.
60. Moore L, Byard RW. Fatal paradoxical embolism to the left carotid artery during partial resection of Wilms' tumor. *Pediatr Pathol* 1992;**12**:551–6.
61. Byard RW, Schliebs J, Koszyca BA. Osler-Weber-Rendu syndrome – pathological manifestations and autopsy considerations. *J Forensic Sci* 2001;**46**:698–701.
62. Pellegrino PA, Zanesco L, Battistella PA. Coagulopathies and vasculopathies. In: Raimondi AJ, Choux M, Di Rocco C, editors. *Cerebrovascular diseases in children*. New York: Springer-Verlag; 1992. p. 189–204.
63. Perkovič-Benedik M, Zaletal M, Pečarič-Meglič N, Podnar T. A right-to-left shunt in children with arterial ischaemic stroke. *Arch Dis Child* 2011;**96**:461–7.
64. Champ C, Byard RW. Pulmonary embolism and unexpected death in infancy. *J Paediatr Child Health* 1994;**30**:550–1.